The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000314.8(PTEN):c.100G>C (p.Ala34Pro)

Version: 1.0

CA377784451

822002 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: e1a14c4d-454d-4af9-86fb-25448ea8dea2
Approved on: 2025/12/5
Published on: 2025/12/19

HGVS expressions

NM_000314.8:c.100G>C
NM_000314.8(PTEN):c.100G>C (p.Ala34Pro)
NC_000010.11:g.87894045G>C
CM000672.2:g.87894045G>C
NC_000010.10:g.89653802G>C
CM000672.1:g.89653802G>C
NC_000010.9:g.89643782G>C
NG_007466.2:g.35607G>C
ENST00000700029.2:c.100G>C
ENST00000710265.1:c.100G>C
ENST00000472832.3:c.100G>C
ENST00000688158.2:n.899+13607G>C
ENST00000688922.2:c.100G>C
ENST00000700021.1:c.100G>C
ENST00000700022.1:c.100G>C
ENST00000706954.1:c.100G>C
ENST00000706955.1:c.*135G>C
ENST00000686459.1:c.100G>C
ENST00000688158.1:c.*275+13607G>C
ENST00000688308.1:c.100G>C
ENST00000693560.1:c.619G>C
ENST00000371953.8:c.100G>C
ENST00000371953.7:c.100G>C
ENST00000462694.1:n.102G>C
ENST00000610634.1:c.-3G>C
NM_000314.5:c.100G>C
NM_000314.6:c.100G>C
NM_001304717.2:c.619G>C
NM_001304718.1:c.-606G>C
NM_000314.7:c.100G>C
NM_001304717.5:c.619G>C
NM_001304718.2:c.-606G>C

Pathogenic

Met criteria codes 5

PP2 PP3 PM2 PS3 PS4

Evidence Links 1

Expert Panel

PTEN VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.100G>C (p.Ala34Pro) meets criteria to be classified as pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (ACMG Classification Rules Specified for PTEN Variant Curation version 3.1.0). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PS3: Phosphatase activity <50% of wild type Phosphatase activity ≤ -1.11 per Mighell et al. 2018 (PMID: 29706350). This variant: score of-3.02. Post 2020-yeast experiments (PMID 32350270)doesn't conflict with Mighell et al 2018) PM2_P: Absent in large sequenced populations PP3_P: REVEL score > 0.7 (score of this variant =0.962) PS4_P:Proband(s) with phenotype specificity score of 1-1.5. (internal laboratory contributor:Organization ID: 26957) PP2: PTEN is defined by the PTEN Expert Panel as a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease.

Met criteria codes

PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✔	REVEL score is 0.962
PM2	✔	Absent in population databases
PS3	✔	In a massively parallel functional assay using a humanized yeast model, lipid phosphatase activity for this variant was functionally deficient (Mighell TL et al. Am J Hum Genet, 2018 May;102:943-955). Score is -3.02 Post 2020 shows damaging effects in yeast experiments A34P- Pred High Impact ,SNAP2-82, CADD Phred-28.6, ASD-N, Somatic-N,#times in COSMIC-0, PHTS-N, GnomAD v2.1.1AF-0, ExAC Allele Freq-0 PubMed:32350270
PS4	✔	1 child with macrocephaly and juvenile polyp. Pediatric score of 5 -1pt 1 person with a history of breast cancer in early 40s- 2pts

Curation History

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